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## Case Report

## Prevalence of periodical leg movements in patients with narcolepsy in an outpatient facility in São Paulo

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## ABSTRACT

Studies have pointed out that approximately 50–60% of narcolepsy patients may demonstrate higher prevalence of periodical leg movements. However, we highlight that the prevalence studies and the effects of periodical leg movements in patients with narcolepsy are limited and with conflicting results. The objective of this study was that of describing and discussing the prevalence of periodical leg movements in patients with narcolepsy in the outpatient facility of diurnal excessive sleepiness of the Federal University of São Paulo, Brazil.

We revised 59 files of patients with the clinical and electrophysiological diagnosis of narcolepsy according to the American Academy of Sleep Medicine.

Of these 59 cases of patients with narcolepsy, 12 (20.3%) demonstrated periodical leg movements. Thirty five patients (59.3%) had history of cataplexy and 38 patients (64.4%) had the presence of the allele HLA-DQB1\*0602. There was a higher prevalence of periodical leg movements in patients with cataplexy ( $p < 0.0001$ ) and in patients with the presence of the allele HLA-DQB1\*0602 ( $p < 0.0001$ ).

Our study characterized the higher prevalence of periodical leg movement in patients with narcolepsy, mainly in patients with cataplexy and with the presence of the allele HLA-DQB1\*0602.

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## 1. Introduction

Narcolepsy is a neurological disease characterized by diurnal excessive sleepiness, cataplexy, hypnagogic hallucinations sleep paralysis and sleep fragmentation. Patients show the first signs and symptoms between the first and second decade of life with a disease prevalence varying in the general populations between 0.025% and 0.05% [1]. Primary sleep diseases such as the restless leg syndrome and periodical leg movements (PLM) have been associated with narcolepsy [2]. However, we point out that the prevalence studies and the effects upon the periodical leg movements in patients with narcolepsy are limited and with conflicting results [3,4].

PLMs are rare among young people and are more common among the aged ones in the general population. PLMs are characterized by a short and rhythmic extension (duration of 0.5–10 s), mainly in the legs, with a minimal series of 4 consecutive movements with intervals between 4 and 90 s [5]. Frequently, PLMs are associated with awakenings and also with several sleep disorders including the restless leg syndrome, sleep obstructive apnea syndrome, sleep behavioral disorder of REM sleep, insomnia and narcolepsy [6]. The PLMs are considered normal in adults up to a frequency of 15 movements per hour during sleep. However, studies that evidenced higher prevalence of PLM in patients with narcolepsy used the index of normalcy limit for PLM at the value of 5 per hour [2,3,7–9].

The objective of this study is to describe and discuss the prevalence of PLM in patients with narcolepsy that were treated at the reference outpatient facility of Sleep Medicine in the city of São Paulo, utilizing the same diagnostic criteria of previous articles.

## 2. Methodology

We have revised the files of 59 patients with clinical and electrophysiological diagnosis of narcolepsy according to the American Academy of Sleep Medicine, who were treated at the outpatient facility of Diurnal Excessive Sleepiness of the Federal University of São Paulo [10,11]. All patients were treated between 2003 and 2013. This article was approved by the Ethical Research Committee of the Federal University of São Paulo (1802/07). Patients were considered as having PLM when five or more movements per hour were present according to the criteria utilized by previous articles about the same topic [2,3,8].

## 3. Statistics

For statistical analysis we used the Chi-square test to verify the association between PLMs and cataplexy, and also for the association between PLM and the allele HLA-DQB1\*0602. Student's t test was used to verify the existence of a possible effect of PLM over the average latency sleep time, as well as the effect of PLM upon the number of REM sleep episodes, during the test of multiple latency sleep time (MLST).

The value of  $p < 0.05$  was considered as significant. The confidence interval was of 95%.

## 4. Results

The anthropomorphic data can be observed in Table 1. Of a total of 59 patients with narcolepsy, 12 (20.3%) did show PLMs.

Thirty five patients (59.3%) had history of cataplexy and 38 patients (64.4%) had the presence of allele HLA-DQB1\*0602. There was a higher prevalence of PLMs with cataplexy ( $p < 0.0001$ ) and in patients with the presence of allele HLA-DQB1\*0602 ( $p < 0.0001$ ).

The results of the multiple latency of sleep tests can be found in Table 1.

There was no difference between the patients with or without PLMs in association with the average latency of MLST ( $3.8 \pm 0.54$  vs.  $3.6 \pm 0.79$ ;  $p = 0.2$ ) and the number of REM sleep episodes ( $2.84 \pm 0.19$  vs.  $3.20 \pm 0.42$ ;  $p = 0.99$ ).

## 5. Discussion

Our study has characterized a high prevalence of PLMs in patients with narcolepsy, mainly among patients with cataplexy and with the presence of allele HLA-DQB1\*0602.

Worsening on the sleep architecture in PLMs patients has been well described with increase in the index of awakenings higher than 5 per hour, associated with PLMs. This limit of 5 per hour index for PLMs to separate normalcy from disorder, is supported by a cohort study of 503 patients performed by Harsh and cols. This study demonstrated a lower sleep efficiency with higher index of awakenings in patients with narcolepsy and PLMs above 5 movements per hour [12]. The increase in the prevalence of PLMs leads to a negative impact upon the quality of sleep and worsens even more than the diurnal somnolence in these patients. The increase of the awakening indexes and superficial sleep stages are already part of the REM sleep instability phenomena frequently described in narcolepsy, which worsens even more during PLMs, leading to a further reduction of the sleep efficiency [7,13].

Although there is no clear association between narcolepsy and PLMs, some studies demonstrated the important role of hypocretin-1 in this association. Alteration of the autonomic regulation, sleep fragmentation and increase in the PLMs prevalence might be present in patients with narcolepsy and cataplexy, although there are controversies in the literature [13]. Apparently there is an autonomic dysfunction which is characterized on the awakenings related to PLMs in patients with narcolepsy and hypocretin system dysfunction [14].

**Table 1 – Anthropomorphic data.**

Age (years)	30.02 ± 18.35
Gender (male)	34 (57.6%)
IMC (Kg/m <sup>2</sup> )	24.8 ± 4.30
Epworth scale	18 ± 3.9
TMLS latency	1.85 ± 1.48 min
SOREMP	2.5 ± 1.27

The decrease in dopamine has an important role in the physiopathology of PLMs [15]. The association between genetic and environmental physiopathologies has gained strength with the discovery of genes and with the iron-related weight on the dopamine production and control of PLMs [16,17]. Alterations of the dopaminergic system may appear to be present in patients with narcolepsy as well. Dogs with narcolepsy and cataplexy demonstrate a higher prevalence of PLMs. These studies demonstrate that the D2/D3 receptors suffer deregulation, which contributes to the episodes of cataplexy. These findings might contribute to the understanding of this possible physiopathological interaction between narcolepsy and PLMs [9,18].

The limitations of this study were the reduced number of patients, the retrospective character of the study and the absence of hypocretin-1 levels in these patients. However, due to the scarce number of studies in this area, we believe that this article might contribute to the research of this very intriguing topic.

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